

Office Action Summary

Application No.

10/583,706

Applicant(s)

MITANI ET AL.

Examiner

STEPHANIE K. MUMMERT

Art Unit

1637

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 August 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-912)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date See Continuation Sheet
- 4) ☒ Interview Summary (PTO-413)
Paper No(s)/Mail Date 2010819
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :3/15/10;4/13/10;5/25/10;7/26/10;11/22/10;12/8/10;12/29/10.

DETAILED ACTION

Applicant's amendment filed on August 16, 2010 is acknowledged and has been entered. Claims 8-83 have been canceled. Claims 1-7 are pending.

Claims 1-7 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is made FINAL as necessitated by IDS.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on May 25, 2010, July 26, 2010, November 22, 2010, December 8, 2010 and December 29, 2010 were filed in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

The information disclosure statement filed March 15, 2010 and April 13, 2010 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of the demandant brief that is not in the

English language. It has been placed in the application file, but the information referred to therein has not been considered.

The information disclosure statement filed October 12, 2010 fails to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement. The information disclosure statement has been placed in the application file, but the information referred to therein has not been considered.

New Grounds of Rejection as necessitated by IDS filed May 25, 2010 – citation to WO96/001327

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rabbani et al. (EP0971039A2, published January 12, 2000) in view of David et al. (WO96/001327; January 1996). Rabbani teaches a set of primers for the amplification of a target (Abstract).

With regard to claim 1, Rabbani teaches a primer set comprising at least two primers that allows a target nucleic acid sequence to be amplified, wherein a first primer included in the primer set contains, in its 3' end portion, a sequence (Ac') that hybridizes to a sequence (A) located in the 3' end portion of the target nucleic acid sequence, and also contains, on the 5' side of the sequence (Ac'), a sequence (B') that hybridizes to a complementary sequence (Bc) to a sequence (B) that is present on the 5' side with respect to the sequence (A) in the target nucleic acid sequence (Figure 4, step 1 and 2, where the first primer includes a sequence F at 3' end complementary to the F' portion at the 3' end of the template, and a sequence E' that is complementary to the E sequence that is 5' with respect to F in the target; and where F and E are equivalent to and in the same format and locations as the regions designated A, B, C, D in the template/target).

With regard to claim 2, Rabbani teaches an embodiment of claim 1, further comprising a third primer that hybridizes to the target nucleic acid sequence or the complementary sequence thereto, wherein the third primer does not compete with other primers for hybridization to the target nucleic acid sequence or the complementary sequence thereto (Figure 2, step 1, primer F, which binds to an extension product of the second primer of claim 1, including the folded sequence).

With regard to claim 3, Rabbani teaches an embodiment of claim 1, wherein in the first primer, when no intervening sequence is present between the sequence (Ac') and the sequence (B'), a ratio $(X-Y)/X$ is in a range of -1.00 to 1.00, where X denotes the number of bases contained in the sequence (Ac') while Y indicates the number of bases contained in a region flanked by the sequence (A) and the 30 sequence (B) in the target nucleic acid sequence, and when an intervening sequence is present bet the sequence (Ac') and the sequence (B') in the primer, a ratio $\{X-(YY')\}/X$ is in a range of -1.00 to 1.00, where X and Y denote the same as described above, and Y' indicates the number of bases contained in the intervening sequence (see Example 1, p. 21, paragraphs 117-118, where the first primer has an F region (corresponding to Ac') of 29 or 30 nucleotides and since there is no intervening sequence between F and E (corresponding to A and B), where the flanking region is 0 nucleotides. Therefore, $(X-Y)/X = (29-0)/29 = 1$).

With regard to claim 4, Rabbani teaches the second primer, the folded sequence (D-Dc') has a length of 2 to 1000 nucleotides (p. 21, paragraph 118, where the stem loop structure depicted in Figure 4, where the basepair stems are 30 bp and 29 or 30 bp loops, leading to a folded sequence of approximately 90 bp).

With regard to claim 5, Rabbani teaches an embodiment of claim 1, wherein at least one primer included in the primer set has a solid-phase support or a site that can bind to a solid-phase support (p. 19, paragraph 103, where the primer includes a group that is useful for attachment of signal generating groups which can also be useful for binding to other formats, including a solid support).

Regarding claim 1, while Rabbani teaches a variety of secondary primers which could easily be combined with the first primer and while Rabbani teaches primers which when extended will form a stem or hairpin structure (see Figure 4, Figure 9), these primers do not have a fold-back portion precisely as claimed.

With regard to claim 1, David teaches a second primer included in the primer set contains, in its 3' end portion, a sequence (Cc') that hybridizes to a sequence (C) located in the 3' end portion of a complementary sequence to the target nucleic acid sequence, and also contains, on the 5' side of the sequence (Cc'), a folded sequence (D-Dc') that contains, on the same strand, two nucleic acid sequences that hybridize to each other (Figure 1, 2, 5, where the second primer includes a region P-P' which forms a folded sequence at the 5' end of the primer and a sequence S in the 3' end of the primer which hybridizes to the sequence S on the template).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the teachings of Rabbani to include the known alternative hairpin primer format of David to arrive at the claimed invention with a reasonable expectation for success. As noted above, while Rabbani does not teach the specific hairpin as claimed, Figure 4 of Rabbani alone suggests a combination of primers which includes the first primer, as noted above and a second sequence at the opposite end of the template or extension product

which includes a folded hairpin sequence. Further, as taught by Rabbani, "the initial primer or nucleic acid construct and the second primer or nucleic acid construct can be the same, or they can be different" (paragraph 43, p. 8). Considering this, it would have been obvious to one of skill to substitute in a variety of secondary primers of different sequence and structure than the initial primer described as the first primer in the invention claimed herein, including a particular hairpin primer as taught by David. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have extended the teachings of Rabbani to include the known alternative hairpin primer format of David to arrive at the claimed invention with a reasonable expectation for success.

Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rabbani et al. (EP0971039A2, published January 12, 2000) in view of David et al. (WO96/001327; January 1996) as applied to claims 1-5 above in view of Pastinen et al. (Genome Research, 1997, vol. 7, p. 606-614). Rabbani teaches a set of primers for the amplification of a target (Abstract).

With regard to claim 5, Rabbani teaches an embodiment of claim 1, wherein at least one primer included in the primer set a site that can bind to a solid-phase support (p. 19, paragraph 103, where the primer includes a group that is useful for attachment of signal generating groups which can also be useful for binding to other formats, including a solid support).

Regarding claim 5, while Rabbani teaches a site for attachment to a solid phase support, Rabbani does not teach attachment to a solid phase support. Pastinen teaches attachment of primers to solid phase support prior to mini-sequencing reactions (Abstract).

With regard to claim 5, Pastinen teaches an embodiment of claim 1, wherein at least one primer included in the primer set has a solid-phase support or a site that can bind to a solid-phase

support (p. 610, col. 2, where oligonucleotide primers were spotted onto a glass slide, attached by a 5' amino group).

With regard to claim 6, Pastinen teaches an embodiment of claim 5, wherein the solid-phase support is one selected from the group consisting of a water-insoluble organic polymer support, a water-insoluble inorganic polymer support, a synthetic polymer support, a phase transition support, a metal colloid, and a magnetic particle (p. 610, col. 2, where oligonucleotide primers were spotted onto a glass slide, attached by a 5' amino group).

With regard to claim 7, Pastinen teaches an embodiment of claim 5, wherein the site that can bind to a solid-phase support is selected from the group consisting of biotin, avidin, streptavidin, an antigen, an antibody, a ligand, a receptor, a nucleic acid, and a protein (p. 610, col. 2, where oligonucleotide primers were spotted onto a glass slide, attached by a 5' amino group).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Rabbani and David to include the attachment of primers to solid phase supports as taught by Pastinen to arrive at the claimed invention with a reasonable expectation for success. As taught by Pastinen, "mutations are detected by extending immobilized primers that anneal to their template sequences immediately adjacent to the mutant nucleotide positions with single labeled dideoxynucleoside triphosphates using a DNA polymerase" (Abstract). Pastinen also teaches, "Our results show that single-nucleotide primer extension is an excellent reaction principle for multiplex detection of mutations" (p. 607, col. 2). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have adjusted the teachings of Rabbani and David to

include the attachment of primers to solid phase supports as taught by Pastinen to arrive at the claimed invention with a reasonable expectation for success.

Conclusion

No claims are allowed. All claims stand rejected.

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on May 25, 2010 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **STEPHANIE K. MUMMERT** whose telephone number is (571)272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stephanie K. Mummert/
Primary Examiner, Art Unit 1637

SKM